19/9/12

ELSEVIER

The Science of the Total Environment 204 (1997) 263–270

the Science of the Total Environment
An International Journal for Scientific Research into the Environment and its Relationship with Man

Population-based biomonitoring in the Czech Republic — the system and selected results

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Received 18 December 1996; accepted 17 June 1997

Abstract

In the framework of the system of monitoring the environmental impact on population health, the concentration of lead, cadmium and selenium in blood and cadmium in urine was measured in adults ($n = 670$), children ($n = 599$) and umbilical blood ($n = 549$) using atomic absorption spectrophotometry. Furthermore, cytogenetic analysis of peripheral lymphocytes in all population groups under study was investigated. The median blood Pb level for the overall group of adults (47.8 μg/l, i.e. 0.23 μmol/l) was significantly higher in men (51.5 μg/l, i.e. 0.25 μmol/l). Smoking significantly influenced the blood Pb level in women. The 90th percentile in no group exceeded the value of 100 μg/l (0.48 μmol/l). The median blood Cd level in adults (0.9 μg/l, i.e. 0.008 μmol/l) depends on smoking habit (1.25 μg/l, i.e. 0.01 μmol/l). The median urine Cd level was 0.585 μg/g creatinine (0.59 μmol/mole creatinine) in adults and 0.37 μg/g creatinine (0.37 μmol/mole creatinine) in children. The median blood Se level (53.5 μg/l, i.e. 0.68 μmol/l) was found to be higher in the group of non-smokers (57.5 μg/l, i.e. 0.73 μmol/l). Lead and selenium level were significantly lower in the umbilical blood. Cytogenetic analysis results showed age-dependent average percentages of aberrant cells: 1.1% in umbilical blood, 1.27% in children and 1.71 in adults in line with the reference values for the Czech population. © 1997 Elsevier Science B.V.

Keywords: Biomonitoring; Lead; Cadmium; Selenium; Blood and urine levels; Cytogenetic analysis

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PII S0048-9697(97)00186-1

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1. Introduction

During the last decade, many countries in Europe have developed or strengthened mechanisms for environmental and health protection. Likewise in the Czech Republic, a system of monitoring the environmental impact on population health in relation to the Plan of Action for the Environment and Health for Europe has been developed (System Monitoring the Environmental Impact on Population Health, 1996). The system has been implemented according to a decree of the government of the Czech Republic from 1991 and involves six projects (air pollution, drinking water quality, noise, dietary exposure, biological monitoring, demographic and health statistics). All projects have been routinely run since 1994.

Biomonitoring has been used to evaluate exposure and risks for various environmental pollutants by means of biomarkers of exposure (internal dose) and biomarkers of effects. The project of biological monitoring includes the monitoring of toxic substances (traces elements, such as lead, cadmium, mercury and arsenic, and organic substances, such as polychlorinated biphenyls, chlorinated pesticides, aflatoxin B1 and ochratoxin) or metabolites (1-OH pyrene, 3-OH benzo[*a*]pyrene and aflatoxin M1) chosen according to their toxicological importance and contemporary scientific knowledge. Besides that, selected essential trace elements (chromium, copper, selenium and zinc) in body fluids and other biological tissues of the Czech population are also studied as biomarkers of population saturation with benefit elements. The cytogenetic analysis of human peripheral lymphocytes in population groups has been used as a biomarker of both exposure to genotoxic clastogens and early biological effect of exposure.

The aim of the project is to assess human exposure to environmental pollutants in the Czech population, to establish the reference values for different population groups, to compare the obtained results with critical and limit values, to determine the most vulnerable population groups, to collect the necessary information for risk assessment and risk management and to help formulate the environmental health policy in the Czech Republic.

In this paper, selected results concerning the levels of lead, cadmium and selenium in blood, cadmium in urine and the cytogenetic analysis results are presented.

2. Material and methods

2.1. Subjects and sampling

Biological monitoring has been implemented in four out of 30 districts put into the entire monitoring system — two of them represent more industrial (the cities of Ústí and Plzeň), the other two more agricultural and recreational living conditions (the cities Benešov and Žďár).

In 1995, the population groups under study were as follows: adults (blood donors): 77% males, 23% females, 41% smokers, mean age, 32 years and mean length of residence in the district, 24 years; children: 51% boys, 49% girls, mean age, 9.3 years and mean length of residence in the district, 8 years (45% of the children lived in families with one or more smokers); newborns (mother's mean age, 26 years, 11% smokers). All blood donors invited to the blood donation in the spring and autumn period who fulfilled the requirements (e.g. age 20–45 years, residence in city at least 3 years, no medication, X-ray examination, viral infection or vaccination within 3 months prior to sampling) were enrolled. The sex disproportion occurred due to fewer female blood donors. Prior to the beginning of the study the subjects' informed consent was obtained. A questionnaire was administered to each subject to ascertain age, weight, height and individual lifestyle (smoking habit, passive smoking exposure, residence in district and profession). Children were contacted through schools and their parents were informed about the project, asked for their consent and for the completion of the questionnaire in advance. Approx. 10% refused to give blood. The exact number of analyzed subjects, sex and smoking habits are presented in tables.

A detailed standard operation protocol for sampling, storage and transport of biological samples was devised. Sampling of blood and urine in adults and children was held in the spring

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(March–May) and the autumn (September–October) period, umbilical blood has been continuously collected throughout the year. Blood samples in the amount of approx. 5 ml were collected using Monovettes for trace element analysis (Sarstedt 02.1065.400) containing heparin as an anticoagulant agent and appropriated siliconized needles. All of the blood samples were immediately thoroughly mixed at room temperature. Samples of 2 ml were taken for cytogenetic analysis and the residual amount was stored at −20°C prior to metal analysis. Spot morning urine samples were collected in polyethylene containers, preliminary washed with 10% nitric acid and demineralized water and stored at −20°C. The aliquots of each urine sample was used for the determination of creatinine by a modified method of Jaffe (Szadkowski et al., 1970).

2.2. Materials

Polyethylene and polypropylene tubes and sample cups were cleaned by 10% HNO_3 and by demineralized water prior to the analysis. Standards of metals under study were prepared by the dilution of the commercial stock standard solution (concentration of analyte 1.00 g/l), Analytika Prague, Czech Republic. Nitric acid Suprapur 65% and Perhydrol 30% G.R. (Merck, Darmstadt, Germany) were used for the mineralization of the samples. Deionized water was produced by the Millipore Purification System. Control materials Seronom NY 904, batch no. 404107 (whole blood) and Seronom NY 115, batch no. 101021 (trace elements urine) were used as control materials.

2.3. Analysis of metals

Samples of blood (1 ml) were mineralized in a microwave oven (CEM MDS 2000) using 5 ml of concentrated HNO_3 and 1 ml of 30% H_2O_2 mixture according to the program described in the manual. After mineralization the excess of the acidic mixture was evaporated to the volume of approx. 0.1 ml and diluted by demineralized water to the final volume (5 ml). For the determination of Cd in urine, samples were diluted threefold with 0.65% HNO_3 before measurement.

Cadmium and Pb in all types of samples were determined by AAS-furnace technique, using a Perkin Elmer 4100 ZL (THGA with integrated Lvov platform) spectrometer and $NH_4H_2PO_4$ as a matrix modifier. Ashing temperatures were 700°C for Cd and 850°C for Pb (atomizing temperature 1500°C for both analytes). The peak area was chosen for the evaluation. The detection limit was 0.2 μg Cd/l, 5 μg Pb/l and 4 μg Se/l for blood and 0.1 μg Cd/g creatinine for urine. Selenium was determined by hydride generation technique using Perkin Elmer 3300 spectrometer in combination with FIAS 400 and hydrochloric acid and natrium borohydride as a reductant agent (recommended analysis conditions for FIM/H analyses).

For the internal quality control the control samples (reference materials) were periodically analyzed with each set of samples (one control per 20 samples). Results of analysis of control samples (Cd 0.7 μg/l, Pb 35.1 μg/l and Se 75 μg/l in the whole blood, Cd 0.29 μg/l in the urine) were in agreement with reported values (Cd 0.7 μg/l, Pb 34 μg/l and Se 80 μg/l in the whole blood, Cd 0.35 μg/l in the urine). Blank samples were run simultaneously (one blank per 10 samples). Evaluation of the stability of the system was provided using internal control samples for the construction of Shewhart control charts.

2.4. Cytogenetic analysis

The cytogenetic analysis of human peripheral lymphocytes was performed on short-term cultures according to modified procedure described by Hungerford (1965). The cultivation time was 52 h with all cells being in the first division. Slides were coded before analysis and blind-scored under 1000 × magnification. One hundred well-spread metaphases per culture were analyzed according to the classification by Bucton and Evans (1973). Only metaphases containing 46 centromeres were analyzed. Four categories of chro-

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mosome aberrations were evaluated: chromatid and chromosome breaks, chromatid and chromosome exchanges. Gaps were not scored as aberrations. Cells bearing breaks or exchanges were designated as aberrant cells.

2.5. *Statistical analysis*

All statistical analyses were undertaken using EPI INFO, Version 6 using the Kruskal–Wallis test.

3. Results

The results of blood lead concentration (PbB) are presented in Table 1 in terms of median and selected percentiles for each overall population group studied as well as stratified according to sex and smoking habit. The age- and sex-dependent differences in PbB levels were observed with a significantly higher PbB in males ($P < 0.01$) and significantly lower ($P < 0.01$) in umbilical blood. An insignificantly higher level in smoking men, but significantly higher level ($P < 0.05$) in women was observed. In children, no sex-dependent differences were observed. The smoking of parents or other persons in children's home did not influence the PbB results. The 90th percentile in all groups was below the value of 100 μg/l (0.48 μmol/l). This value was exceeded in 1.3% ($n = 7$) of umbilical blood samples, 2.2% ($n = 13$) of investigated children and 5.7% ($n = 38$) of adults.

The results of blood (CdB) and urine (CdU) cadmium concentration are summarized in Table 2. The level of CdB in adults depends on the smoking habit ($P < 0.01$) but no influence of passive smoking was observed in children. To correctly evaluate the Cd concentration in urine it is necessary to take into account the degree of dilution of the urine. Therefore the concentration of creatinine was determined and all CdU results are expressed per g of creatinine. A significantly lower CdU level ($P < 0.01$) was observed in children.

Table 3 contains the results of blood selenium concentrations (SeB). Lower SeB was observed in smokers. The SeB was surprisingly higher in children from the families with smokers ($P < 0.05$). The lowest level of selenium ($P < 0.01$) was found in umbilical blood.

The cytogenetic analysis results (Table 4) reflect age-dependence with the lowest mean number of aberrant cells in the umbilical blood and highest in adults. The results were not influenced by smoking habit.

4. Discussion

Biological monitoring has long tradition in the assessment of occupational exposure but in the

Table 1
Selected percentiles of blood lead distribution (in μg/l) according to sex and smoking habit in monitored population groups (1995)

Groups	Percentiles						
	n	2.5	10	50	90	97.5	Range
Umbilical blood	549	4.2	7.9	27.7**	58.4	77	2.0–241
Children total	599	9.4	13.7	39.7	97.2	100	0.4–340
Boys	309	9.8	13.5	38.7	98.6	100	6.1–340
Girls	290	9.1	13.9	40.6	95.4	100	0.4–252
Smoking family	270	9.8	15.0	40.4	100	104	0.4–340
Non-smoking family	329	8.5	13.1	39.6	90.7	100	6.1–252
Adults total	668	9.2	21.0	47.8	96.5	148	3.2–360
Males	515	10.2	23.5	51.5	97.2	156	3.6–358
Females	153	6.6	16.9	40.0	94.2	110	3.2–159
Smokers	275	13.1	24.0	50.6*	97.4	149	3.6–250
Non-smokers	393	7.9	18.1	45.0	95.6	136	3.2–358

* $P < 0.05$ (smokers vs. non-smokers).
** $P < 0.01$ (umbilical blood vs. other groups).

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Table 2
Selected percentiles of blood (in μg/l) and urine (in μg/g creatinine) cadmium distribution according to sex and smoking habit in monitored population groups (1995)

Groups	Percentiles						
	n	2.5	10	50	90	97.5	Range
Cd in blood							
Umbilical blood	411	0.10	0.31	0.60	1.60	2.15	0.10–4.7
Children total	599	0.15	0.15	0.70	4.00	7.19	0.15–13.0
Boys	308	0.15	0.15	0.80	4.00	7.00	0.15–13.0
Girls	291	0.15	0.15	0.64	4.00	7.98	0.15–12.3
Smoking family	270	0.15	0.15	0.61	4.00	7.00	0.15–12.3
Non-smoking family	329	0.15	0.15	0.80	4.00	7.98	0.15–13.0
Adults total	670	0.15	0.30	0.90	2.84	4.92	0.10–15.4
Males	516	0.15	0.30	0.95	3.00	5.00	0.10–13.7
Females	154	0.15	0.33	0.80	2.00	4.04	0.15–15.4
Smokers	276	0.30	0.60	1.25**	3.00	5.13	0.15–10.0
Non-smokers	394	0.15	0.15	0.65	2.00	4.04	0.10–15.4
Cd in urine							
Children total	632	0.060	0.083	0.370**	1.29	2.51	0.005–10.4
Boys	327	0.066	0.085	0.394	1.24	2.83	0.005–10.4
Girls	305	0.060	0.080	0.360	1.31	2.32	0.005–7.8
Smoking family	280	0.060	0.091	0.389	1.29	2.24	0.005–4.5
Non-smoking family	352	0.060	0.080	0.360	1.28	2.83	0.005–10.4
Adults total	604	0.055	0.099	0.585	2.05	4.61	0.005–10.7
Males	465	0.054	0.092	0.550	2.08	5.22	0.310–10.7
Females	139	0.081	0.178	0.699	1.96	3.13	0.005–5.8
Smokers	244	0.058	0.137	0.650	1.89	4.05	0.362–10.2
Non-smokers	360	0.055	0.097	0.550	2.14	5.14	0.005–10.7

** $P < 0.01$ (smokers vs. non-smokers, children vs. adults).

Table 3
Selected percentiles of blood selenium distribution (in μg/l) according to sex and smoking habit in monitored population groups (1995)

Groups	Percentiles						
	n	2.5	10	50	90	97.5	Range
Umbilical blood	350	5.0	25.0	34.5**	58.7	69.2	4.0–82.6
Children total	388	17.1	27.1	49.6	72.2	84.3	5.0–98.2
Boys	196	16.1	26.5	48.5	71.9	80.3	10.0–94.5
Girls	192	19.3	29.5	50.6	73.3	87.6	5.0–98.2
Smoking family	190	22.3	27.1	51.6*	71.9	81.8	10.0–87.3
Non-smoking family	198	16.3	28.0	48.1	72.4	88.9	5.0–98.2
Adults total	468	10.2	31.4	53.5	75.8	95.1	3.2–136
Males	340	10.1	30.6	53.5	74.1	96.1	3.2–136
Females	128	14.1	34.5	53.3	82.4	92.7	3.2–120
Smokers	192	10.2	30.4	48.1*	70.6	87.2	3.2–136
Non-smokers	276	9.5	32.6	57.5	81.5	101.9	3.2–120

* $P < 0.05$ (smokers vs. non-smokers).
** $P < 0.01$ (umbilical blood vs. other groups).

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Table 4
Frequency of chromosomal aberrations (%) in the monitored population groups (1994–1995)

Group	n	Arith. mean (%)	S.D. (%)	Range	CI
Umbilical blood	421	1.11	1.17	0–7	1.00–1.21
Children	1139	1.27	1.33	0–11	1.19–1.33
Adults	762	1.71	1.36	0–8	1.63–1.74

last years it has been used more often for estimating total human exposure to environmental pollutants (Aitio, 1994). Before the political changes in 1989 in the former Czechoslovakia, possible consequences of environmental pollution and health problems were not clearly documented. The need for a more systematic and large scale studies seems to have been fulfilled with the implementation of the system of monitoring the environmental impact on population health (summary report, 1996).

The level of toxic metals in human tissues may represent the important indicator of the health status. The earlier data obtained in the Czech studies are mostly unsuitable for exposure assessment because they usually did not meet the recently designed criteria (Kučera et al., 1995). Lead is one of the most widely dispersed toxic substances of this century. Despite reductions in the amount of lead added to the environment over the past 20 years, even lower exposure level is considered hazardous and are of great public health concern. Recent evidence from epidemiological studies points to the potentially long-lasting effects of in utero exposure on neurobehavioral and cognitive development of children (Davis and Svensgaard, 1987). Surveys of the adult general population with mean PbB levels around 150 μg/l observed positive associations between PbB and blood pressure (Harlan, 1988).

The level of lead in blood is the best available indicator of current and recent past environmental exposure and may also be a reasonably good indicator of lead body burden with stable exposure. A critical level 100 μg/l (0.48 μmol/l) of lead in blood of small children was proposed, based on population studies (WHO, 1994). The PbB values obtained in our population groups were considerably lower than those reported for populations from different countries in the late 1970s and 1980s (Huel et al., 1986, Krause et al., 1989, Kučera et al., 1995) and did not show any significant body burden of our population. An observed higher level in men and the relationship of PbB to smoking was also found in other studies (Krause et al., 1989).

According to IARC, cadmium and cadmium compounds are classified as class 1 human carcinogens. Besides that, Cd may affect renal function (Kjellström et al., 1977). For biological monitoring blood and urine cadmium levels are used. Blood cadmium generally reflects current exposure and the levels are usually between 0.2 and 0.8 μg/l (0.0018–0.007 μmol/l). Considerably higher concentrations (1.4–4.5 μg/l, i.e. 0.012–0.04 μmol/l) are observed in smokers (Elinder et al., 1994). In our monitored population groups, even in non-smokers, the median level of Cd (0.65 μg/l, i.e. 0.006 μmol/l) was observed to be generally higher than in populations in other countries (Schwarz et al., 1993) with the additional increase in smokers and indicate the significance of exposure and body burden. Cadmium in the urine is a measure of cumulative exposure in the past with usual levels between 0.1 and 0.7 μg/g of creatinine (0.1–0.7 μmol/mole creatinine). In our population groups the value 2 μg Cd/g creatinine (2.02 μmol/mole creatinine) which is considered a maximal tolerable population internal dose (Buchet et al., 1990) was exceeded in 11.2% of adults and 6.3% of children. No sex- or smoking-related differences were observed. Little difference in cadmium level in umbilical blood and blood of adults may indicate that this metal can move rather freely through the human placenta (Ong et al., 1993).

Selenium belongs to the essential trace elements with the relation to risk of heart disease and cancer (Salonen et al., 1984; Salonen et al., 1989). Measurements of selenium in serum and blood are usually taken in order to identify a possible deficiency and reflect the levels of dietary selenium intake. The selenium level in

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serum is usually between 60 and 120 μg/l, the concentration in red cells is somewhat higher than in plasma (Elinder et al., 1994). Our results with whole blood selenium levels indicating that the selenium status of our monitored groups is relatively low, below the European average, are in agreement with previous data obtained for the Czech population (Korunová et al., 1993). Lower blood selenium concentration seems to be related to smoking habit. No explanation was found for a significant higher Se level in the group of children from families with smokers.

Cytogenetic analysis of human peripheral lymphocytes is frequently used to document the early biological effect resulting from exposure to mutagens and carcinogens (Legator and Au, 1994). There is suggestive evidence that groups with increased chromosomal aberrations may have an increased risk of cancer (Hagmar et al., 1994). This method has a long tradition in the Czech Republic (Rössner et al., 1995) and ranks among the standard methods used for biological monitoring of occupational exposure to genotoxicants for more than 15 years. The results presented here are in agreement with the reference values valid for our population and did not show any increased exposure to genotoxic pollutants.

Summarizing our results, it is possible to conclude that the monitoring activities to date afford the information needed to establish reference values of several trace elements and chromosomal changes in the Czech population and represent the basis for the perspective evaluation of developmental trends in longer temporal series.

Acknowledgements

The authors appreciate the contribution of the field coordinators and technicians from the Institutes of Hygiene in Benešov, Brno, Plzeň, Prague, Ústí and Žďár to the success of this survey. They also thank Dr. E. Švandová for the statistical analysis. This work was supported by the Government of the Czech Republic and in part by the research grant IGA No. 2764-3 of the Czech Ministry of Health.

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